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OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

MEMORANDUM

DATE: 10 MARCH 2010

SUBJECT: FIPRONIL – Nondietary Exposure/Risk Assessment for the Proposed Use of Fipronil in Termidor® Dry Termiticide.

PC Code:	129121	**DP Barcode:**	D372250
MRID No.:	None	**EPA Reg. No.**	Not Reg'd.
Petition No.:	None	**Regulatory Action:**	Section 3
Assessment Type:	ORE	**Reregistration Case No.:**	None
TXR No.:	None	**CAS No.:**	120068-37-3

FROM: Mark I. Dow, Ph.D., Biologist
Alternate Risk Integration Assessment Team (ARIA)
Risk Integration Minor Use & Emergency Response Branch (RIMUERB)
Registration Division (RD) 7505P

THROUGH: John C. Redden, ARIA Team Leader JCR
RIMUERB/RD 7505P

TO: Clayton Myers, Risk Manager
Insecticides Branch
RD 7505P

INTRODUCTION

Under provisions in Section 3 of the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA), as amended, the BASF Corporation has requested registration of the insecticide active ingredient (ai) fipronil (PC No. 129121; CAS No. 120068-37-3) for use as a termiticide.

The risk assessment techniques used in this document are those that have been developed and refined by the HED/Office of Pesticide Programs' Science Policy Council for Exposure (ExpoSAC). RD herein utilizes the same techniques as are HED's standard operating procedures (SOP).

3/17/2010

USE PATTERN SUMMARY

The product proposed for registration is known as Termidor® Dry Termiticide (EPA Reg. No. 7969-XXX). It is formulated as a dry, "dispersible" powder. The formulated product contains 0.5 % by weight, fipronil ai. It should be noted that fipronil is currently registered for use as a termiticide (Termidor® 80 WG Termiticide/Insecticide, Reg. No. 7969-209; Termidor® SC Termiticide/Insecticide, Reg. No. 7969-210).

Unlike the WG and SC formulations, Termidor® Dry Termiticide is not designed to be prepared and applied as a liquid spray application. Termidor® Dry Termiticide is formulated in "precharged" glass vials which are attached to a squeeze bulb dust application device. Since patents are pending, a detailed description is not presented as the design is considered proprietary business information.

As noted, the vials are charged (i.e., loaded) by the formulator. The charged vials are presealed prior to shipment. The vials are attached to the application devise by twisting/threading on like jar lid. As the vial is attached, a seal is punctured and the vial is "activated" for use. The vials contain 5.0 gram formulation which is 0.5 % active ingredient fipronil. The vials are not refillable by the user and the label directs users NOT to refill the vials.

The product is labeled for sale to, and use and storage only by individuals/firms licensed or registered by each state to apply termiticide and/or general pest control products. The intended use is to control subterranean and drywood termites.

Application sites include structural voids and damaged wood galleries, shelter tubes, termite nests or other inaccessible areas of buildings, trees, utility poles, fencing, decking materials, railroad trestles, piers, beams and other structural or landscape timbers where termite damage is observed or termite activity is present or suspected.

The draft product label indicates that approximately 3 applicator bulb compressions deliver 0.1 g of product formulation. The label also states: "Do not apply more than 5 grams per 1,000 ft^2.

For drywood termites, the product should be applied at a rate of 0.1 – 1.0 g of Termidor® Dry Termiticide per injection point.

For subterranean termites, the label suggests application of 0.1 – 1.0 g per injection point in termite galleries and shelter tubes. For application to carton nests, applications should be 0.3 – 3.0 g per injection point. For application into construction voids, the rate is 0.2 – 2.0 g per injection point.

If termite activity persists after application, reapplication may occur 30 days after previous application.

OCCUPATIONAL PESTICIDE HANDLER EXPOSURE

Based upon the proposed use pattern, RD believes that applicators will be exposed during application of the product. There is no mixing or loading in the typical sense since the vials are loaded, i.e., charged by the formulator. Further, post-application exposure is not expected as the material is to be injected into hollows or voids that are not accessible to humans.

Typically, the Agency utilizes information in the Pesticide Handler Exposure Database (PHED) Surrogate Exposure Guide (v. 1.1, August 1998) to assess occupational pesticide exposures (exposures to mixers, loaders, applicators). In this case, there are no data specific to the proposed use pattern with which to estimate exposure. Therefore, for purposes of a conservative, screening level assessment, the PHED unit exposure for a mixer/loader using open-pour loading of a wettable powder, is used as a surrogate. RD believes that the use of the mixer/loader unit exposure will likely result in overestimation of actual exposure from the proposed use pattern and thus to overestimation of risk. The draft label does not contain directions for the use of any personal protective equipment (PPE) thus estimates are presented for an individual wearing long pant, long sleeved shirt, shoes plus socks and with or without the use of protective gloves.

In addition, in order to "bracket" the exposure estimate, RD also uses the unit exposure for a resident loader/applicator applying pesticide dust to a home garden. In the latter case, the unit exposure is for an individual wearing long pants, short sleeved shirt and no protective gloves. The unit exposure is taken from an Outdoor Residential Exposure Taskforce study (MRID 44459801). BASF Corp. is a member of the ORETF.

The toxicological factors used in this assessment are taken from: Memo, M. Dow, 18 DEC 2007, DP Code 346777. The Agency identified a short-term duration (1 - 30 days) dermal toxicological endpoint from a 21-day dermal toxicity study in the rabbit. The No Observable Adverse Effects Level (NOAEL) is 5.0 mg ai/kg bw/day and the toxic effects noted were decreased body weight gain and food consumption in both sexes. A 70 kg body weight is used to calculate dermal exposure. Since the dermal toxicological endpoint was identified from a dermal study, there is no adjustment for dermal absorption. The level of concern (LOC) for dermal exposures is for Margins of Exposure (MOE) < 100.

A short-term duration inhalation endpoint was identified from a developmental neurotoxicity study in the rat. The NOAEL is 0.05 mg ai/kg bw/day and the toxic effects seen were decreases in group mean pup weights during lactation and significant increase in time of preputial separation in males. Since the inhalation toxic effects were identified from a developmental study with fetal effects, a 60 kg bw is used to calculate inhalation exposure. HED and RD assume 100% absorption via the inhalation route of exposure. See Table 1.0 for a summary of estimated exposures and risks and see the ATTACHMENT for a summary of toxicological endpoints used for risk assessment.

Due to the nature of the proposed use pattern and to anecdotal information available to the Agency, RD believes exposures will be short-term (1-30 days). Further, RD has no information regarding a "typical work" day or "typical amounts" of formulation per day that might be applied using the proposed application methodology. Therefore, to be conservative, it is assumed that an applicator will contact the entire contents of a vial. Typically, applicators may utilize an applicator over a period of days or weeks before needing to attach a new, charged vial.

Table 2.0 Summary of Exposure & Risk to Occupational Handlers From Applying Termidor® Dry Termiticide

Unit Exposure[1] mg ai/lb handled	Applic. Rate[2] lb ai/unit	Units Treated[3]	Avg. Daily Exposure[4] mg ai/kg bw/day	MOE[5]	Combined[6] MOE
Unit Exposure From: *(PHED) Mixer/Loader – Wettable Powder- Open Pour*					
Dermal:	5 gm/vial	1 vial/day	Dermal:	No Glove	No Glove
SLNoGlove 3.7	@0.5% ai		SLNoGlove 0.0000029	1.7 million	770,000
SLWithGlove 0.17	0.000055 lb ai		SLWithGlove 0.000000134	With Glove	With Glove
Inhal. 0.04				37.3 million	1.3 million
			Inhal. 0.000000037	1.4 million	
Unit Exposure From: *(ORETF) Resident Loader/Applicator – Garden Dust*					
Dermal:	5 gm/vial	1 vial/day	Dermal:	No Glove	No Glove
Long pants, short	@0.5% ai		SLNoGlove 0.000086	58,000	35,000
sleeves, NO gloves 110	0.000055 lb ai		Inhal. 0.00000057	88,000	
Inhal. 0.62					

1. Unit Exposures are taken from "PHED SURROGATE EXPOSURE GUIDE", Estimates of Worker Exposure from The Pesticide Handler Exposure Database Version 1.1, August 1998. Dermal = Single Layer Work Clothing **No Gloves**; Single Layer Work Clothing **With Gloves**; Inhal. = Inhalation. Resident Loader Applicator Unit Exposure from ORETF study MRID 4449801. Units = mg a.i./pound of active ingredient handled
2. Applic. Rate. = assumed since unknown.
3. Units Treated = assumed one vial per day
4. Average Daily Dose = Unit Exposure * Applic. Rate * Units Treated ÷ (70 kg bw dermal) (60 kg bw inhalation)
5. MOE = Margin of Exposure = NOAEL ÷ ADD. Dermal NOAEL 5.0 mg/kg bw/day; Inhalation NOAEL 0.05 mg/kg bw/day.
6. Combined MOE = Combined MOE is expressed as $1/(1/MOE_{DERMAL} + 1/MOE_{INHALATION})$.

A MOE of 100 is adequate to protect occupational pesticide handlers from exposures to fipronil. The estimated MOEs are all > 100. Therefore the proposed new uses do not exceed RD's level of concern. It should be noted that the unit exposures used in this case for risk assessment are considered to be conservative, i.e., protective. Actual exposure and risk that result from the proposed use pattern is expected to be lower than what has been estimated and presented above.

As was noted earlier, RD has no information regarding "typical" use per day. In other countries where the product is registered, a vial is not totally dispensed over the course of several days. In view of the Margins of Exposure, multiple vials could be used per day and not exceed the Agency's level of concern.

POST-APPLICATION EXPOSURE TO AGRICULTURAL WORKERS

In most pesticide application situations, post-application exposure is possible and likely. However, in this particular case, post-application exposure is not expected. The material is to be "injected" into structure voids or into termite galleries or tree holes infested with termites. As such, the possibility of post-application exposure is believed to be negligible. In view of the Margins of Exposure to an applicator (i.e., large numbers), it is not likely that any post-application that 'might' occur would be equal to, or greater than that experienced by an applicator. Post-application exposure is thereby not assessed and is not believed to be of concern.

ATTACHMENT

Acute Toxicity Data on *FIPRONIL*

Guideline No./ Study Type	MRID No.	Results	Toxicity Category
870.1100 Acute oral toxicity -rat	42918628	LD50 = _ 92/_ 103 mg/kg; _+_ 97 mg/kg	II
870.1200 Acute dermal toxicity	42918629 42918630	LD50 = > 2000 mg/kg [rat] = 354 mg/kg [rabbit]	III II
870.1300 Acute inhalation toxicity -rat	43544401	LC50 = _ 0.36/_ 0.42 mg/L; _+_ 0.39 mg/L	II
870.2400 Acute eye irritation -rabbit	42918632	mild transient ocular irritant	III
870.2500 Acute dermal irritation - rabbit	42918633	slight dermal irritant	IV
870.2600 Skin sensitization -Guinea Pig	42918634	non-sensitizing	

Summary of Toxicological Dose and Endpoints for Fipronil for Use in Human Risk Assessment [1].

Exposure Scenario (Fipronil)	Dose Used in Risk Assessment, UF	FQPA SF and Endpoint for Risk Assessment	Study and Toxicological Effects
Acute Dietary all populations	NOAEL= 2.5 mg/kg	FQPA SF = 1 **aPAD** = acute RfD	Acute neurotoxicity - rat LOAEL = 7.0 mg/kg based on: decreased

including infants and children	UF = 100 **Acute RfD** = 0.025 mg/kg	FQPA SF = 0.025 mg/kg	hindleg splay in males at 7 hours.
Chronic Dietary <u>all populations</u>	NOAEL= 0.019 mg/kg/day UF = 100 **Chronic RfD** = 0.0002 mg/kg/day	FQPA SF = 1 **cPAD** = <u>chr RfD</u> FQPA SF = 0.0002 mg/kg/d	Chronic/carcinogenicity study - rat LOAEL = 0.059 mg/kg/day based on: increased incidence of seizures and death, alterations in clinical chemistry (protein), increased TSH, and decreased T4.
Short-Term Oral (1-7 days) (Residential)	oral study LOAEL ≤0.1 mg/kg/day UF of 3 for no NOAEL, 100 for interspecies extrapolation and intraspecies variation	**LOC for MOE** = 300 (Residential, includes the FQPA SF)	Developmental toxicity Study - rabbit LOAEL = ≤ 0.1 mg/kg/day based on: maternal toxicity of decreased body weight gain, decreased food consumption, and decreased food efficiency.
Intermediate-Term Oral (1 week - several months) (Residential)	oral study LOAEL ≤0.1 mg/kg/day UF of 3 for no NOAEL, 100 for interspecies extrapolation and intraspecies variation	**LOC for MOE** = 300 (Residential, includes the FQPA SF)	Developmental Toxicity Study - rabbit LOAEL = ≤ 0.1 mg/kg/day based on: maternal toxicity of decreased body weight gain, decreased food consumption, and decreased food efficiency.
Short-Term Dermal (1-7 days) (Occupational/ Residential)	dermal study NOAEL= 5 mg/kg/day	**LOC for MOE** = 100 (Occupational) **LOC for MOE** = 100 (Residential, includes FQPA SF)	21-Day dermal toxicity study - rabbit LOAEL = 10.0 mg/kg/day based on: decreased body weight gain, and food consumption in both sexes.
Intermediate-Term Dermal (1 week - several months) (Occupational/ Residential)	dermal study NOAEL= 5 mg/kg/day	**LOC for MOE** = 100 (Occupational) **LOC for MOE** = 100 (Residential, includes FQPA SF)	21-Day dermal toxicity study - rabbit LOAEL = 10.0 mg/kg/day based on: decreased body weight gain, and food consumption in both sexes.
Long-Term Dermal (several months - lifetime) (Occupational/ Residential)	oral study NOAEL= 0.019 mg/kg/day (dermal absorption rate = 1%)	**acceptable MOE** = 100 (Occupational) **acceptable MOE** = 100 (Residential, includes FQPA SF)	Chronic/carcinogenicity study - rat LOAEL = 0.059 mg/kg/day based on: increased incidence of seizures and death, alterations in clinical chemistry (protein), increased TSH, and decreased T4.
Short-Term Inhalation (1-7 days) (Occupational/	oral study NOAEL= 0.05 mg/kg/day (inhalation absorption rate =	**LOC for MOE** = 100 (Occupational) **LOC for MOE** = 100 (Residential, includes	Developmental neurotoxicity - rat LOAEL = 0.90 mg/kg/day based on: decrease in group mean pup weights during lactation, and significant increase in time of preputial separation in males (dietary).

Residential)	100%)	FQPA SF)	
Intermediate-Term Inhalation (1 week - several months) (Occupational/ Residential)	oral study NOAEL= 0.05 mg/kg/day (inhalation absorption rate = 100%)	**LOC for MOE** = 100 (Occupational) **LOC for MOE** = 100 (Residential, includes FQPA SF)	Developmental neurotoxicity - rat LOAEL = 0.90 mg/kg/day based on: decrease in group mean pup weights during lactation, and significant increase in time of preputial separation in males (dietary).
Long-Term Inhalation (several months - lifetime) (Occupational/ Residential)	oral study NOAEL= 0.019 mg/kg/day (inhalation absorption rate = 100%)	**acceptable MOE** = 100 (Occupational) **acceptable MOE** = 100 (Residential, includes FQPA SF)	Chronic/carcinogenicity rat study LOAEL = 0.059 mg/kg/day based on: increased incidence of seizures and death, alterations in clinical chemistry (protein), increased TSH, and decreased T4.
Cancer (oral, dermal, inhalation)	Group C - possible human carcinogen	Use chronic RfD to estimate human risk	Increases in thyroid follicular cell tumors with fipronil (male/female)

[1] UF = uncertainty factor, FQPA SF = FQPA Safety Factor, NOAEL = no observed adverse effect level, LOAEL = lowest observed adverse effect level, PAD = population adjusted dose (a = acute, c = chronic) RfD = reference dose, LOC = level of concern, MOE = margin of exposure.

cc:M.Dow(RIMUERB)
RDI:J. Redden, M. Clock-Rust
M.I.Dow:S7824:PY1:(703)305-5533:RIMUERB:7505P

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